

CLAIMS

What is claimed is:

1. A nucleic acid molecule that down regulates expression of CLCA1 (Chloride Channel Calcium Activated) gene.
- 5 2. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is used to treat conditions selected from the group consisting of Chronic Obstructive Pulmonary Disease (COPD), chronic bronchitis, asthma, cystic fibrosis, and obstructive bowel syndrome.
- 10 3. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is an enzymatic nucleic acid molecule.
4. The nucleic acid molecule of claim 3, wherein a binding arm of said enzymatic nucleic acid molecule comprise sequences complementary to any of sequences having SEQ ID NOs:1-2189 and 5399-5416.
- 15 5. The nucleic acid molecule of claim 3, wherein said enzymatic nucleic acid molecule comprises any of sequences having SEQ ID NOs:2190-5398 and 5425-5434.
6. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is an antisense nucleic acid molecule.
- 20 7. The nucleic acid molecule of claim 6, wherein said antisense nucleic acid molecule comprises sequences complementary to any of sequences having SEQ ID NOs:1-2189 and 5399-5416.
8. The nucleic acid molecule of claim 6, wherein said antisense nucleic acid molecule comprise any of sequences having SEQ ID NOs:5417-5424.
- 25 9. The nucleic acid molecule of claim 3, wherein said enzymatic nucleic acid molecule is in a hammerhead (HH) motif.
10. The nucleic acid molecule of claim 3, wherein said enzymatic nucleic acid molecule is in a hairpin, hepatitis Delta virus, group I intron, VS nucleic acid, amberzyme, zinzyme or RNase P nucleic acid motif.

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11. The nucleic acid molecule of claim 3, wherein said enzymatic nucleic acid molecule is in an Inozyme motif.
12. The nucleic acid molecule of claim 3, wherein said enzymatic nucleic acid molecule is in a G-cleaver motif.
- 5 13. The nucleic acid molecule of claim 3, wherein said enzymatic nucleic acid molecule is a DNAzyme.
14. The nucleic acid molecule of claims 3 or 6, wherein said nucleic acid molecule comprises between 12 and 100 bases complementary to RNA of a CLCA1 gene.
- 10 15. The nucleic acid molecule of claims 3 or 6, wherein said nucleic acid molecule comprises between 14 and 24 bases complementary to RNA of a CLCA1 gene.
16. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is chemically synthesized.
- 15 17. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises at least one 2'-sugar modification.
18. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises at least one nucleic acid base modification.
19. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises at least one phosphate backbone modification.
- 20 20. A mammalian cell comprising the nucleic acid molecule of claim 1.
21. The mammalian cell of claim 20, wherein said mammalian cell is a human cell.
22. A method of reducing CLCA1 activity in a cell, comprising the step of contacting said cell with the nucleic acid molecule of claim 1, under conditions suitable for said reduction of CLCA1 activity.
- 25 23. A method of treatment of a patient having a condition associated with the level of CLCA1, comprising contacting cells of said patient with the nucleic acid molecule of claim 1, under conditions suitable for said treatment.

24. The method of claim 23 further comprising the use of one or more therapies under conditions suitable for said treatment.
25. A method of cleaving RNA of a CLCA1 gene, comprising contacting the nucleic acid molecule of claim 3 with said RNA under conditions suitable for the cleavage of said RNA.
26. The method of claim 25, wherein said cleavage is carried out in the presence of a divalent cation.
27. The method of claim 26, wherein said divalent cation is  $Mg^{2+}$ .
28. The nucleic acid molecule of claim 1, wherein said nucleic acid comprises a cap structure, wherein the cap structure is at the 5'-end or 3'-end or both the 5'-end and the 3'-end.
29. The enzymatic nucleic acid molecule of claim 9, wherein said hammerhead motif comprises sequences complementary to any of sequences having SEQ ID NOs:1-575.
30. The enzymatic nucleic acid molecule of claim 11, wherein said Inozyme motif comprises sequences complementary to any of sequences having SEQ ID NOs:576-1210.
31. The enzymatic nucleic acid molecule of claim 12, wherein said G-cleaver motif comprises sequences complementary to any of sequences having SEQ ID NOs:1211-1429.
32. The enzymatic nucleic acid molecule of claim 13, wherein said DNAzyme comprises sequences complementary to any sequence shown as substrate sequences in Table VII.
33. The enzymatic nucleic acid molecule of claim 10, wherein said zinzyme comprises sequences complementary to any sequence shown as substrate sequences in Table VI.
34. The enzymatic nucleic acid molecule of claim 10, wherein said amberzyme comprises sequences complementary to any sequence shown as substrate sequences in Table VIII.
35. An expression vector comprising at least one nucleic acid molecule of claim 1, in a manner that allows expression of the nucleic acid molecule.

36. A mammalian cell comprising an expression vector of claim 35.
37. The mammalian cell of claim 36, wherein said mammalian cell is a human cell.
- 5 38. The expression vector of claim 35, wherein said nucleic acid molecule is an enzymatic nucleic acid molecule.
39. The expression vector of claim 35, wherein said expression vector further comprises an antisense nucleic acid molecule complementary to RNA of a CLCA1 gene.
- 10 40. The expression vector of claim 35, wherein said expression vector comprises at least two said nucleic acid molecules.
41. The expression vector of claim 40, wherein the at least two nucleic acid molecules are the same.
42. The expression vector of claim 40, wherein the at least two nucleic acid molecules are different.
- 15 43. The expression vector of claim 40, wherein one said expression vector further comprises an antisense nucleic acid molecule complementary to RNA of a CLCA1 gene.
44. The expression vector of claim 40, wherein one said expression vector further comprises an enzymatic nucleic acid molecule complementary to RNA of a CLCA1 gene.
- 20 45. A method for treatment of chronic obstructive pulmonary disease comprising the step of administering to a patient the nucleic acid molecule of claim 1 under conditions suitable for said treatment.
- 25 46. A method for treatment of cystic fibrosis comprising the step of administering to a patient the nucleic acid molecule of claim 1 under conditions suitable for said treatment.
47. An enzymatic nucleic acid molecule that cleaves RNA derived from a CLCA1 gene.

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48. The enzymatic nucleic acid molecule of claim 47, wherein said enzymatic nucleic acid molecule is selected from the group consisting of Hammerhead, Hairpin, Inozyme, G-cleaver, DNAzyme, Amberzyme and Zinzyme.
- 5 49. The method of claims 45 or 46, wherein said method further comprises administering to said patient the nucleic acid molecule of claim 1 in conjunction with one or more other therapies.
- 10 50. The method of claim 49, wherein said other therapies are therapies selected from the group consisting of oxygen therapy, bronchodilators, corticosteroids, antibacterials, vaccinations, acetylcysteine, mucokinetic agents, and DNase (Pulmozyme) treatments.
- 15 51. The nucleic acid molecule of claim 9, wherein said nucleic acid molecule comprises at least five ribose residues, at least ten 2'-O-methyl modifications, and a 3'- end modification.
52. The nucleic acid molecule of claim 51, wherein said nucleic acid molecule further comprises a phosphorothioate core with both 3' and 5' -end modifications.
53. The nucleic acid molecule of claims 51 or 52, wherein said 3' and/or 5'- end modification is 3'-3' inverted abasic moiety.
- 20 54. The nucleic acid molecule of claim 3, wherein said nucleic acid molecule comprises at least five ribose residues; at least ten 2'-O-methyl modifications, and a 3'- end modification.
55. The nucleic acid molecule of claim 54, wherein said nucleic acid molecule further comprises phosphorothioate linkages on at least three of the 5' terminal nucleotides.
- 25 56. The nucleic acid molecule of claim 54, wherein said 3'- end modification is 3'-3' inverted abasic moiety.
57. The enzymatic nucleic acid molecule of claim 13, wherein said DNAzyme comprises at least ten 2'-O-methyl modifications.
- 30 58. The enzymatic nucleic acid molecule of claim 57, wherein said DNAzyme further comprises phosphorothioate linkages on at least three of the 5' terminal nucleotides.

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59. The enzymatic nucleic acid molecule of claim 57, wherein said DNAzyme further comprises a 3'-end modification.
60. The enzymatic nucleic acid molecule of claim 59, wherein said 3'- end modification is 3'-3' inverted abasic moiety.